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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,408	12/12/2003	Richard Storer	06171.105064 IDX 1024	2099
20786	7590	09/24/2008		
KING & SPALDING LLP 1180 PEACHTREE STREET ATLANTA, GA 30309-3521			EXAMINER KRISHNAN, GANAPATHY	
			ART UNIT	PAPER NUMBER
			1623	
			MAIL DATE	DELIVERY MODE
			09/24/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/735,408

**Applicant(s)**

STORER ET AL.

**Examiner**

Ganapathy Krishnan

**Art Unit**

1623

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 20, 32, 36, 37 and 108-134 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20, 32, 36-37 and 108-134 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_



### **DETAILED ACTION**

The amendment filed 7/7/2008 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-19, 21-31, 33-35 and 38-107 have been canceled.
  2. New Claims 108-134 have been added.
  3. Claims 20 and 36 have been amended.
  4. Remarks drawn to claim objections and rejections under 35 USC 112, second paragraph and 103 and a Declaration under 37 CFR 1.132 by Adel Moussa.
- Claims 20, 32, 36-37 and 108-134 are pending in the case.

### ***Claim Objections***

The objection to Claims 35 and 102 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim has been rendered moot by cancellation of the said claims.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 36 and 92 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been overcome by amendment of claim 36 and cancellation of claim 92. Applicants have stated in their remarks that claim 92 has also been

amended. But in the Amendments to the Claims, the status of claims 38-107 are indicated as cancelled.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of Claims 20, 32, 36-37 and 108-134 under 35 U.S.C. 103(a) as being unpatentable over BeMiller et al (Methods in Carbohydrate Chemistry, 1963, 2, 484-485, IDS document # HK) in combination with The Merck Index (12<sup>th</sup> edition, 1996, pages 274-275), Ault (Techniques and Experiments for Organic Chemistry, 5<sup>th</sup> Edn., 1987, 105-113), Sundberg et al (Advanced Organic Chemistry, Part B, 1990, pages 232 and 235-236), McFarlin (J. Am. Chem. Soc. 1958, 80, 5372-76) and Piccirilli et al (J. Org. Chem. 1999, 64, 747-54; IDS document # HH) is being maintained for reasons of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants' have traversed the rejection under 35 USC 103(a) of record in the previous action arguing that:

1. The Examiner has provided no reason why one of skill in the art would modify the process of BeMiller to use the specific step of adding CaO to a solution of fructose. BeMiller's process works for the intended purpose without the use of CaO. BeMiller does not teach that the solubility of calcium hydroxide is an important part of the process.

2. Piccirilli does not teach the preparation of 2-C-methyl-D-ribofuranose. He references an earlier publication which uses an entirely different process.

3. The claims are not obvious since applicants have shown unexpected results with regard to yield, reaction times and ease of purification.

Applicants' arguments and the Declaration by Adel Moussa have been considered but are not found to be persuasive.

The Merck Index teaches that calcium oxide is soluble in water forming calcium hydroxide (page 275, entry # 1733) but calcium hydroxide is only slightly soluble in water (page 274, entry # 1716). This is the reason why BeMiller adds calcium hydroxide to the hot solution.

Reacting aqueous CaO with fructose as instantly claimed is same as the reaction taught by BeMiller et al. The use of calcium oxide is also preferable in view of Merck Index since it is more soluble in water and dissolves to produce the calcium hydroxide needed for the said conversion. No heating is necessary. The dissolution of calcium oxide in water is also exothermic and the heat generated will help dissolve any undissolved starting materials. This is a practical convenience that one of ordinary skill in the art will recognize. BeMiller doesn't necessarily have to teach the importance of the solubility of calcium hydroxide in the process. BeMiller's may have worked for its intended purpose without the use of CaO. This doesn't mean that it cannot and should not be modified. The modification by using CaO for practical reasons is a reasonable modification. Given the higher solubility of CaO in water and it forming calcium hydroxide on dissolution would give the aqueous solution of calcium hydroxide in the required concentration without having to use calcium hydroxide as such and heating it to dissolve in water.

Piccirilli et al teach the use of benzoyl derivative of ribofuranose (page 748, structure 1) in synthesis of 2'-branched nucleosides. He also discloses that 2'-alkyl substituted ribofuranoses are useful for the syntheses of 2'-C-branched nucleosides since such nucleosides show cytotoxicity towards leukemic cell lines and might be useful in gene regulation (see introduction). This means that a synthesis of protected 2'-C-branched ribofuranoses from readily available starting materials like D-fructose would be very useful. One of skill in the art would also extend the instant process to protected ribofuranoses since Piccirilli teaches the use of such protected sugars for the synthesis of nucleosides. Hence one of skill in the art would want to extend the instant process to include protected sugars. Piccirilli need not teach the same process.

Any given process can be extended to include the preparation of structurally close analogs. This is routine and is known to one of ordinary skill in the art.

Applicants have claimed unexpected results with regard to yield, reaction times and ease of purification and have provided a Declaration by Adel Moussa. According to applicants it is unexpected that the use of a ratio of calcium oxide to D-fructose of 4 to 1, 2 to 1 and 1.5 to 1 gave higher product yields in shorter times than the corresponding process of BeMiller, which uses calcium hydroxide. Perusal of the Table at page 3 of the Declaration shows that the yield of the products are 13.4%, 13.6% and 13% respectively for reaction times of 22.25 hrs, 20.5 hours and 22.25 hours. This is not seen as an unexpected result. BeMiller's process gives an yield of 10%. The Declaration shows just a 3% improvement in yield if the reaction is carried out for a period of 22-26 hours, which is comparable to that reported by BeMiller. The shorter reaction time has not produced a substantial improvement in the yield of the product. Applicants have stated that instant claim 36 has been amended to recite simplified process for purifying the ribonolactone and that the crude product obtained via the instant process is easier to purify compared to that of BeMiller who uses ion exchange. Amended claim 36 recites standard procedures of filtration and extraction used in organic syntheses for isolation and purification process. This is also taught by Ault and one of ordinary skill in the art would use such steps to isolate and purify the product. Applicants have not shown that the product of Bemiller obtained before ion exchange purification is not as good as the instant product via a side by side comparison. Moreover, one of skill in the art would use ion exchange purification as an additional step only if the purity of the product obtained before such a step is not satisfactory.



For solid products as instantly obtained one of skill in the art would use recrystallization for purification. This is routine in the art.

Applicants' arguments and the Declaration of Adel Moussa are not seen to overcome the rejection.

### **Conclusion**

Claims 20, 32, 36-37 and 108-134 are rejected

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/  
Examiner, Art Unit 1623

/Shaojia Anna Jiang, Ph.D./  
Supervisory Patent Examiner, Art Unit 1623